

Amendments to the Specification

Please replace the paragraph beginning at page 1, line 15, with the following rewritten paragraph:

Methods utilizing mass spectrometry for the analysis of a target polypeptide have been taught wherein the polypeptide is first solubilized in an appropriate solution or reagent system. The type of solution or reagent system, e.g., comprising an organic or inorganic solvent, will depend on the properties of the polypeptide and the type of mass spectrometry performed and are well-known in the art (see, e.g. Vorm et al. (1994) Anal. Chem. 66:3281 (for MALDI) and Valaskovic et al. (1995) Anal. Chem. 67:3802 (for ESI)). Mass spectrometry of peptides is further disclosed, e.g. in WO 93/24834 by Chait et al.

Please replace the paragraph beginning at page 37, line 3, with the following rewritten paragraph:

Figure 1 is a photograph of a tricine gel DEAE 3 (Elution) comparing ~~Alzheimers~~ Alzheimer's disease versus Age Matched Control;

Figure 2 is a trypsin digested spectra graph depicting the characteristic profile of the ion 1682 (SEQ ID NO:1); SEQ ID NOS:5-7 and SEQ ID NO:1 are shown in the chart as read from top to bottom;

Figure 3 is a trypsin digested spectra graph depicting the characteristic profile of the ion 2755 (SEQ ID NO:2);

Figure 4 is a photograph of a tricine gel DEAE 5 (Elution) comparing ~~Alzheimers~~ Alzheimer's disease versus Age Matched Control;

Figure 5 is a trypsin digested spectra graph depicting the characteristic profile of the ion 2147 (SEQ ID NO:3); and

Figure 6 is a trypsin digested spectra graph depicting the characteristic profile of the ion 1471 (SEQ ID NO:4).

Please replace the paragraph beginning at page 41, line 12, with the following rewritten paragraph:

DEAE Column Protocol:

- 1) Cast 200 µl of 50% slurry;
- 2) Equilibrate column in 5 bed volumes of 50 mM tricine pH 8.8 (binding buffer);
- 3) Dissolve 25 µl of sera in 475 µl of binding buffer;
- 4) Wash column in 5 bed volumes of binding buffer;
- 5) Elute column in 120 µl of 0.4 M Phosphate buffer (PB) pH 6.1;
- 6) Elute column in 120 µl of 50 mM citrate buffer pH 4.2;
- 7) Scrub column with 120 µl sequentially with each of 0.1% ~~triton~~ TRITON , 1.0% ~~triton~~ TRITON and 2% SDS in 62.5 mM [[Tris]] TRIS pH 6.8.

Please replace the paragraph beginning at page 42, line 3, with the following rewritten paragraph:

Butyl SEPHAROSE column protocol:

- 1) Cast 150 μ l bed volume column;
- 2) Equilibrate column in 5 bed volumes of 1.7 M $(\text{NH}_4)_2\text{SO}_4$ in 50 mM PB pH 7.0 (binding buffer);
- 3) Dissolve 35 μ l of sera in 465 μ l of binding buffer and apply;
- 4) Wash column in 5 bed volumes of binding buffer;
- 5) Elute column in 120 μ l of 0.4 M $(\text{NH}_4)_2\text{SO}_4$ in 50 mM PB pH 7.0;
- 6) Elute column in 120 μ l of 50 mM PB pH 7.0;
- 7) Scrub column with 120 μ l sequentially with each of 0.1% ~~triton~~ TRITON, 1.0% ~~triton~~ TRITON and 2% SDS in 62.5 mM ~~[[Tris]]~~ TRIS pH 6.8.

Please replace the paragraph beginning at page 42, line 18, with the following rewritten paragraph:

Phenyl SEPHAROSE column protocol:

- 1) Cast 150 μ l bed volume column;
- 2) Equilibrate column in 5 bed volumes of 1.7 M $(\text{NH}_4)_2\text{SO}_4$ in 50 mM PB pH 7.0 (binding buffer);
- 3) Dissolve 35 μ l of sera in 465 μ l of binding buffer

and apply;

- 4) Wash column in 5 bed volumes of binding buffer;
- 5) Elute column in 120 μ l of 0.2 M $(\text{NH}_4)_2\text{SO}_4$ in 50 mM PB pH 7.0;
- 6) Elute column in 120 μ l of 50 mM PB pH 7.0;
- 7) Scrub column with 120 μ l sequentially with each of 0.1% ~~triton~~ TRITON , 1.0% ~~triton~~ TRITON and 2% SDS in 62.5 mM [[Tris]] TRIS pH 6.8.

Please replace the paragraph beginning at page 43, line 9, with the following rewritten paragraph:

HiQ Anion Exchange Mini Column Protocol:

- 1) Dilute sera in sample/running buffer;
- 2) Add HiQ resin to column and remove any air bubbles;
- 3) Add ultrafiltered (UF) water to aid in column packing;
- 4) Add sample/running buffer to equilibrate column;
- 5) Add diluted sera;
- 6) Collect all the flow-through fraction in ~~Eppendorf~~ EPPENDORF tubes until level is at resin;
- 7) Add sample/running buffer to wash column;
- 8) Add elution buffer and collect elution in ~~Eppendorf~~ EPPENDORF tubes.

Please replace the paragraph beginning at page 43, line 22, with the following rewritten paragraph:

HiS Cation Exchange Mini Column Protocol:

- 1) Dilute sera in sample/running buffer;
- 2) Add HiS resin to column and remove any air bubbles;
- 3) Add UF water to aid in column packing;
- 4) Add sample/running buffer to equilibrate column for sample loading;
- 5) Add diluted sera to column;
- 6) Collect all flow through fractions in ~~Eppendorf~~ EPPENDORF tubes until level is at resin;
- 7) Add sample/running buffer to wash column;
- 8) Add elution buffer and collect elution in ~~Eppendorf~~ EPPENDORF tubes.

Please replace the paragraph beginning at page 44, line 11, with the following rewritten paragraph:

Illustrative of the various buffering compositions useful in this technique are:

Sample/Running buffers: including but not limited to Bicine buffers of various molarities, pH's, NaCl content, ~~Bis-Tris~~ BIS-TRIS buffers of various molarities, pH's, NaCl content, Diethanolamine of various molarities, pH's, NaCl content, Diethylamine of various

molarities, pH's, NaCl_content, Imidazole of various molarities, pH's, NaCl content, Tricine of various molarities, pH's, NaCl content, Triethanolamine of various molarities, pH's, NaCl content, [[Tris]] TRIS of various molarities, pH's, NaCl content.

Elution Buffer: Acetic acid of various molarities, pH's, NaCl content, Citric acid of various molarities, pH's, NaCl content, HEPES of various molarities, pH's, NaCl content, MES of various molarities, pH's, NaCl content, MOPS of various molarities, pH's, NaCl content, PIPES of various molarities, pH's, NaCl content, Lactic acid of various molarities, pH's, NaCl content, Phosphate of various molarities, pH's, NaCl content, Tricine of various molarities, pH's, NaCl content.

Please replace the paragraph beginning at page 46, line 10, with the following rewritten paragraph:

As a result of these procedures, the disease specific markers, found to be complement component C3 precursors, having a molecular weight of about 1681.7532 daltons and a sequence of SEQ ID NO:1, a molecular weight of about 2755.2910 daltons and a sequence of SEQ ID NO:2, a molecular weight of about 2147.0733 datons and a sequence of SEQ ID NO:3, and ~~complement c3 precursor~~ having a molecular weight of about 1471.7446 daltons having a sequence of SEQ ID NO:4 related to ~~Alzheimers~~ Alzheimer's disease were found.

Please replace the paragraph beginning at page 49, line 11, with the following rewritten paragraph:

The specific disease markers which are analyzed according to the method of the invention are released into the circulation and may be present in the blood or in any blood product, for example plasma, serum, cytolyzed blood, e.g. by treatment with hypotonic buffer or detergents and dilutions and preparations thereof, and other body fluids, e.g. [[CSF]] cerebrospinal fluid (CSF), saliva, urine, lymph, and the like. The presence of each marker is determined using antibodies specific for each of the markers and detecting specific binding of each antibody to its respective marker. Any suitable direct or indirect assay method may be used to determine the level of each of the specific markers measured according to the invention. The assays may be competitive assays, sandwich assays, and the label may be selected from the group of well-known labels such as radioimmunoassay, fluorescent, or chemiluminescence immunoassay or immunoPCR technology. Extensive discussion of the known immunoassay techniques is not required here since these are known to those of ~~skilled~~ skill in the art. See Takahashi et al. (Clin Chem 1999; 45(8): 1307) for a detailed example of an assay.